UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

In re: OXYCONTIN ANTITRUST LITIGATION	04 md. 1603 (SHS) This document relates to: 06 Civ. 13095 (SHS) 07 Civ. 03972 (SHS) 07 Civ. 03973 (SHS) 07 Civ. 04810 (SHS) **NONCONFIDENTIAL VERSION**

MALLINCKRODT'S REPLY BRIEF ON THE UNENFORCEABILITY OF U.S. PATENT NOS. 5,549,912, 5,656,295, and 5,508,042 DUE TO INEQUITABLE CONDUCT

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INTRODUCTION

Purdue's effort to defend the deceptive conduct that led to issuance of the patents in suit—U.S. Patent Nos. 5,549,912 ("the '912 patent"), 5,656,295 ("the '295 patent") and 5,508,042 ("the '042 patent")—involves a purposeful misreading of the procedural posture of this case, an effort to revise what is otherwise a damning factual record, and misrepresentations of what was and was not decided in the *Endo* case.

First, Purdue tries to frame this case as merely an occasion to decide the remand ordered by the Federal Circuit in *Purdue Pharma L.P. v. Endo Pharmaceuticals, Inc.*, 438 F.3d 1123 (Fed. Cir. 2006). Thus, Purdue would have the Court believe that the primary issue is whether the inventors of the patents and their attorneys intended to deceive the Patent Office by portraying Kaiko's insight regarding the alleged four-fold dosage range of controlled-release oxycodone in language implying that this insight was supported by clinical proof, while concealing the absence of such proof. (*Id.* at 4.) Purdue characterizes the *additional* evidence that Mallinckrodt and KV have discussed of other deceptive acts by the inventors and their attorneys as relevant only to the issue of Purdue's intent with respect to Kaiko's "surprising discovery" of the four-fold dosage range. (*Id.* at 23 ("Defendants' additional arguments fail to establish intent to deceive the PTO").)

The present proceeding is not the *Endo* remand. In addition to the *Endo* record, Mallinckrodt has presented a new record, with well-founded accusations of additional deceptive conduct by the inventors and their attorneys in the Patent Office. It is for this Court, as the trier of fact, to assess the materiality of these various acts and the evidence of a pervasive pattern of deceptive intent that they collectively reflect.

While Mallinckrodt will address each of Purdue's arguments, it is important, as a preliminary matter, to identify what this Court and the Federal Circuit did *not* decide in *Endo*. This Court made crystal clear that it was ruling only on Purdue's misrepresentations regarding the purported four-fold dosage range of controlled release oxycodone:

> Because Purdue committed inequitable conduct by misrepresenting its "surprising[ ] discover[y]" of a reduced dosage range, thus rendering the patents in suit invalid, this Court need not decide whether or not Purdue committed other acts of inequitable conduct before the PTO.

Purdue Pharma L.P. v. Endo Pharmaceuticals, Inc., 2004 WL 26523, Case No. 00-cv-8029, at *21, n. 11 (S.D.N.Y. Jan. 5, 2004). That being the case, the Federal Circuit confined its review of the Court's findings and the underlying evidence to the four-fold-dosage-range representations and omissions.

Nevertheless, Purdue asserts that this Court and the Federal Circuit decided more factual issues:

- According to Purdue, "[n]either this Court, nor the Federal Circuit has ever accepted the argument that Purdue had a 'motive to deceive.'" (Purdue Br. at 23-24.) The short response is that neither court even addressed the argument. It is blatantly improper for Purdue to represent, on the basis of judicial silence, that a fact has been found.

- Purdue next asserts that "[b]oth this Court and the Federal Circuit have rejected arguments of inequitable conduct based on Purdue's post-filing clinical studies," i.e. that Purdue committed inequitable conduct in withholding from the Patent Office the results of clinical studies that contradicted Purdue's patentability arguments on reduced dosage range and easier titration. (Purdue Br. at 5-6, 35-39.) While this Court questioned the probative value of Purdue's clinical studies in the context of its consideration of the issue of *infringement* in *Endo* (*Endo,* 2004 WL 26563 at *15), the Court did not address the withholding of the studies from the Patent Office in the context of its discussion of *inequitable conduct.* There is also nothing in the Federal Circuit's opinion on the subject. Once again, a finding cannot be implied from judicial silence.

- Finally, Purdue asserts that both this Court and the Federal Circuit have found that Kaiko's discovery of the purported four-fold dosage range was not the ground on which Purdue overcame the examiner's rejection of the

> '912 patent claims as anticipated by U.S. Patent No. 4,990,341 ("the '341 patent") on controlled-release hydromorphone. (Purdue Br. at 13.) As support for this proposition, Purdue cites the Federal Circuit's discussion of *construction of the patent claims*, not the discussion of *inequitable conduct*.(*Id.* (citing *Endo*, 438 F.3d at 1136).) Moreover, Purdue ignores the Federal Circuit's ruling that, as a matter of law, inequitable conduct may be found whether or not an examiner relies on a material misrepresentation. *Endo*, 438 F.3d. at 1131-32.

The deceptive acts and omissions discussed in this brief demonstrate a disturbing pattern of misconduct that itself provides compelling evidence of an intent to mislead the Patent Office. In evaluating the evidence of intent to deceive with respect to each of these acts of misconduct, the Court is entitled to consider not only the intent evidenced by the individual act, but also the intent evidenced by the multiple acts. *See, e.g.*, *Paragon Podiatry Lab., Inc. v. KLM Labs., Inc.*, 984 F.2d 1182, 1193 (Fed. Cir. 1993) ("The prosecution of the patent application in this case, viewed in its entirety, demonstrates an overriding pattern of misconduct sufficient to support the district court's finding of culpable intent.") Purdue understandably evades any discussion of the disturbing *pattern* of misconduct that pervades this case.

ARGUMENT

I. Purdue has no effective explanation for Kaiko's misrepresentation that, according to surveys of daily dosages of other opioid analgesics, an eight-fold range of daily dosages is required to control pain in 90% of patients.

In its brief, Mallinckrodt established that it was an outright falsehood for Purdue to represent, in each of the specifications of the patents in suit and repeatedly during the prosecution of the '331 patent and the patents in suit, that surveys of other opioid analgesics suggest that they require an eight-fold range of daily dosages in order to control pain in 90% of patients. (*See* Mallinckrodt Br. at 22-28.)

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Purdue does not contest the materiality of these affirmative misrepresentations and, indeed, it cannot. (*See* Purdue Br. at 24-25.) The alleged eight-fold dosage range for other opioid analgesics provides the critical benchmark for establishing the allegedly novel and unexpected reduced, four-fold dosage range. If there is not an eight-fold dosage range for other opioids, the purported four-fold dosage range for controlled-release oxycodone would be neither novel nor unexpected.

Moreover, Purdue does not address the use by its attorneys of the alleged eight-fold dosage range for prior-art controlled-release opioid compositions in responding to office actions rejecting the '331 claims and the '912 claims in light of the prior-art '341 controlled-release hydromorphone patent. (*See* Purdue Br. at 25-26.) As Mallinckrodt has shown, Purdue's attorneys affirmatively represented that an eight-fold dosage range was required for controlled-release hydromorphone of the '341 patent as a reason why that prior-art patent did not render the claims of the '331 patent obvious and a reason why it did not anticipate or render obvious the claims of the '912 patent. (Mallinckrodt Br. at 11, 24-25; *see* Howard Decl., Ex. 27, PTX 7 at '331-41-43.) Purdue asserts that the latter representation played no role in the issuance of the patents in suit, but the truth is exactly the opposition. (Mallinckrodt Br. at 19, 25.)

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Purdue now asserts that the medical literature contained "surveys" of other opiates. (Purdue Br. at 25-26.) Purdue resorts to a 1992 Pain Society monograph mentioned in the patent specifications, but that publication does not deal

* Citations to "Howard Reply Decl., Ex. __" refer to the Declaration of Casey B Howard in Support of Mallinckrodt's Reply Brief on the Unenforceability of U.S. Patent Nos. 5,549,912, 5,656,295, and 5,508,042 Due to Inequitable Conduct attached hereto and includes exhibits 49-60.

with dosage ranges or identify any "surveys" purporting to do so. (*See* Purdue Br. at 4; Inz Decl., Ex. 4.) The monograph cites an article by one Eisenach, reporting that, in surgical patients receiving intravenous, patient-controlled analgesia following caesarian section, the "demand rate" was between 0.6 and 5.2 mg. hourly (an 8.67-fold dosage range). (Inz Decl., Ex. 5 at 445.) Purdue's invocation of that study is misleading. The Eisenach study was intended to compare patient satisfaction with physician-administered intramuscular injections vs. patient-controlled intravenous administration. (*Id.* at 444.) The 8.67-fold dosage range involved morphine only and was reported for patients who *self administer*. (*Id.* at 444-45.) Lower dosage ranges were reported for other routes of administration, including a 4.66-fold dosage range for morphine in combination supplemental morphine or medperidine "as needed." (*Id.* at 445 (observing range of 0.75-3.5 mg/hour).) It also must be noted that none of the four opiates used in this study was hydromorphone, and the study provides no support for the eight-fold dosage range that Purdue's attorneys told the Patent Office was required to control pain in 90% of patients.

Equally, if not more important, Kaiko has never testified that he relied on the Pain Society monograph or the Eisenach article as part of his purported "surveys" It is highly significant that Purdue's attorneys have not submitted an affidavit from Kaiko to that effect.

In the absence of such an affidavit, Purdue's latest story about the non-existent surveys of other opiate analgesics is self-evidently an effort by Purdue's litigation counsel to repair irreparable damage to their case.

II. The Court can find inequitable conduct based solely on Purdue's statement or implication that experimental results supported its "finding" that a four-fold dosage range for controlled-release oxycodone distinguished the patent claims from the prior art.

Mallinckrodt's brief identified four considerations not addressed in this Court's *Endo* opinion that bear on evidence of the intent of the inventors and their attorneys in representing to

the Patent Office that it had been "surprisingly found" that a four-fold dosage range of controlled release oxycodone controls pain in 90% of patients: (1) the language they selected to describe the discovery, always in precise numerical terms and often in the past tense (*see* Mallinckrodt Br. at 20); (2) the knowledge of Kaiko and the other inventors of their duty of candor and honesty in their dealings with the Patent Office (*id.* at 29); (3) the motive that Kaiko, in particular, had to deceive the Patent Office in order to obtain broad patent protection for his insight (*id.*); and (4) the relevance, to the determination of intent, of a pattern of other intentionally deceptive conduct (*id.* at 30).

On point no. 1, while Purdue tries half-heartedly to defend the language used to describe the surprising discovery of the purported four-fold dosage range, nothing Purdue has said provides the Court with any grounds to revisit its analysis of the misleading character of that language or to revisit the Federal Circuit's corresponding analysis in *Endo*. (*See* Purdue Br. at 27.) On point no. 2, Purdue implicitly concedes that the inventors, including Kaiko, knew that they owed a duty of candor and honesty in their dealings with the Patent Office. On Point No. 4, the pattern of deceptive conduct that permeates this case and its relevance to the determination of intent, Purdue is silent.

Purdue is reduced to arguing that there was no motivation to deceive the Patent Office (Purdue Br. at 23-25); that Kaiko truly believed in his insight (*Id.* at 20-21); and that, in any event, the representations regarding the four-fold dosage range played no causal role in the Patent Office's decisions to allow the '331 patent and the patents in suit to issue (*Id.* at 21-23). Each contention is flawed.

On the issue of motivation, Purdue's suggestion that the Court and the Federal Circuit "have never accepted that Purdue had a motive to deceive" is illegitimate. (Purdue Br. at 23.)

To infer from a court's silence that it has actually decided anything on a particular point of argument is a mistake that even a first-year law student would not make. Moreover, Purdue's further argument that Purdue, as a corporate entity, had no motive to deceive misses the point. (*Id.* at 24.) It is neither here nor there that others at Purdue besides Kaiko, who were equally concerned about the imminent onset of generic competition in the market for Purdue's lucrative MS Contin® product, considered other alternatives besides commercialization of controlled-release oxycodone. Mallinckrodt has presented telling evidence that *Kaiko* had a motive to deceive in order to obtain broad patent protection for his pet product, and that is enough. (Mallinckrodt Br. at 29-30; Howard Decl., Ex. 2, *Endo* Tr. at 167-68 (Kaiko), 484 (Oshalck), and 994 (Goldenheim).)

Purdue's further argument, that Kaiko genuinely believed his insight about the four-fold dosage range, is irrelevant. In *Hoffman-LaRoche, Inc. v. Promega Corp.*, 323 F.3d 1354 (Fed. Cir. 2003), the district court found that the inventors believed they had discovered a novel enzyme, but nevertheless held their patent to be unenforceable because the inventors included in the specification an example erroneously stating that that they had performed a particular purification protocol and had obtained certain results. *Id.* at 1363-66. The Federal Circuit affirmed, holding that the inventors' good-faith belief in the novelty of their discovery did not immunize them from a finding of inequitable conduct in these circumstances:

> The inventors may indeed have believed they had discovered a new enzyme, but that belief does not permit them to make misrepresentations in seeking to persuade the examiner to issue a patent for that enzyme. Thus, the district court's finding that the inventors had a good faith belief in the novelty of their invention is not incompatible with a finding of deceptive intent.

Id. at 1367. The same principle applies here.

Further on the issue of motive, it is not true, as Purdue remarks, that all branded pharmaceutical companies have a motive to lie to the Patent Office. (Purdue Br. at 24.) Those

companies with truly meritorious inventions have no motive to deceive a patent examiner. Only those with weak arguments for patentability would have that motive because, if the Patent Office discovered the true facts, the patents might not issue.

Purdue complains that the documents purporting to show that the discovery was not surprising are "not prior art" and cannot establish "even 'prima facie' unpatentability" (Purdue Br. at 27-28), but this is meaningless because patentability is not the issue here. Further, the Court should reject Purdue's red herring of an argument that the memos containing information about what Kaiko expected to find are confidential and thus not prior art. Mallinckrodt does not suggest that Purdue had a duty to disclose the memos. Rather, the memos simply show that Kaiko's "insights" were not surprising at all; to the contrary, they were expected. (*See* Howard Decl., Ex. 21, DTX 3735 (*e.g.*, OxyContin's short half-life is "well established in the literature"; "basic pharmacokinetic principles" show that a short half-life allows for rapid attainment of steady state; "several…studies have established that oxycodone has a high oral bioavailability…" etc., etc.).)

Finally, in a last-ditch argument, Purdue says that, during prosecution of the '331 and '912 applications, the inventors and their attorneys invoked the surprising discovery of the four-fold dosage range only a few times and that Kaiko's discovery did not form the basis on which the patents issued. (Purdue Br. at 22-23.) Drawing upon the prosecution history of the '331 application, Purdue speculates about the reason or reasons why the examiner withdrew his obviousness rejection of the '331 claims based on the combination of the '341 patent for controlled-release hydromorphone and the '598 patent for controlled-release oxycodone. (*Id* at 23..) In similar fashion, Purdue also speculates on the reasons why the examiner withdrew his anticipation rejection of the '912 claims based on the '341 patent. (*Id.* at 21-22.)

Purdue assiduously ignores the fact that, in *Endo*, Federal Circuit has already rejected these arguments as a matter of law:

> Purdue contends it did not make material misrepresentations or fail to disclose material information to the PTO because the examiner did not rely on its assertion of the four-fold dosage range for oxycodone. According to Purdue, the examiner could have allowed the claims based on other arguments it made to distinguish oxycodone over the prior art. Even assuming that the examiner did not necessarily rely on Purdue's discovery of a four-fold dosage range, however, that would not be inconsistent with a finding of materiality.

Endo 438 F.3d at 1131-32, citing *Hoffman-LaRoche*, 323 F.3d at 1368; *Merck & Co. v. Danbury Pharmacal, Inc.*, 873 F.2d 1418, 1421 (Fed. Cir. 1989). There is no "but for" rule of causation in the analysis of inequitable conduct, and a misrepresentation may be the basis of a finding of unenforceability whether or not the examiner in fact relied on it. *See, e.g.*, *Merck & Co.*, 873 F.2d at 1421.

In a related vein, Purdue argues that the patent claims, properly construed, define the invention by specified ranges of blood plasma levels, and that the preambles to these claims, which state the benefit of a reduced dosage range, are not operative limitations. (Purdue Br. at 14.) Therefore, according to Purdue, the four-fold dosage range could not have been material to issuance of the patents. Once again, the Federal Circuit in *Endo* rejected this argument, as a matter of both fact and law, holding, among other things that "materiality is 'not limited to matters reflecting the claims of a patent.'" 438 F.3d at 1132, citing *Hoffman-LaRoche*, 323 F.3d at 1367.

III. It was misleading for Purdue to use the word "surprising" to describe its purported discovery that the disclosed product will provide 12 hours of pain relief in a controlled-release formulation with an early T_{max}.

As explained in Mallinckrodt's opening brief, Purdue's intent to deceive is further established by its repeated use of the word "surprising" to describe that the disclosed oxycodone formulation will provide 12 hours of pain relief in a controlled-release formulation having a T_{max}

of about 2 to 4-1/2 hours. (Mallinckrodt Br. at 33-36.) To support its claim of surprise, Purdue represented that it was "usual in the pharmaceutical art" to produce formulations with a much later (4-8 hour T_{max}) peak plasma level. (Howard Decl., Ex 27, PTX 7 at '331-7.) In our earlier brief, however, Mallinckrodt discussed the fact that Purdue presented no evidence at trial of *any* extended-release composition having a T_{max} of 4 to 8 hours and providing 12 hours of effectiveness. (Mallinckrodt Br. at 33.) It suffices here to note that Purdue *still* has not pointed to any such evidence.

There *was* evidence, however, well known to Purdue, of other controlled-release opioid compositions that, like the controlled-release oxycodone formulation, provided 12 hours of pain relief when the T_{max} was between 2 and 4 hours—at least *four* other such compositions. (*See* Howard Decl., Ex. 11, DTX 2766 (MS Contin®); Ex. 13, DTX 2047 the '984 patent (dihydrocodeine); Ex. 15, DTX 2045 the '341 patent (hydromorphone); Ex. 16, PTX 16 (codeine).) Mallinckrodt asked in its brief whether it can really be a "surprise" the fifth time one formulates a controlled-release opioid composition with these characteristics. (Mallinckrodt Br. at 35.) Purdue answers that it can, but the reasoning it sets forth indicates otherwise.

First, Purdue protests that "'[s]urprising' is a common term in patent prosecution" and that the "mere use" of that term cannot prove intent to deceive. (Purdue Br. at 27.) True, but very much beside the point. *When used accurately*, the mere use of the term "surprising" might not prove intent to deceive. But when something is *not* a surprise and a patent applicant says that it is, and when he goes even further and withholds evidence tending to show that the discovery is not a surprise, that is powerful damning evidence of an intent to deceive the Patent Office.

Purdue further argues that results obtained with one extended-release opioid analgesic—*i.e.*, 12 hours of pain relief with a 2-4 hour T_{max}—will not necessarily be obtained with another

related, albeit structurally slightly different, opioid. (*Id.* at 29.) The argument is unavailing. It might have been "surprising" the *first* time Purdue found that a controlled-release formulation of a structurally different opioid had the same early T_{max} profile and provided 12 hours of pain relief as a prior-art opioid composition. Maybe even a second time. But where the prior art includes no fewer than *four* concededly different opioids that all exhibit the same 12-hour-relief-with-early-T_{max} controlled-release profile, then the fact that oxycodone, hydromorphone, morphine, codeine, and dihydrocodeine are each slightly different from one another ceases to be a distinction upon which to call the result "surprising."

Purdue's further boast that its controlled-release oxycodone formulation is a "research success story" is irrelevant. (*Id.* at 29-30.) The issue here is not obviousness—that is, if need be, for another day. The question here is inequitable conduct, and if Purdue misled the Patent Office in its effort to get the '331 patent and the patents-in-suit, then the patents are unenforceable regardless of patentability. *See, e.g., Duro-Last, Inc. v. Custom Seal, Inc.*, 321 F.3d 1098, 1107 (Fed. Cir. 2003) ("This court has long held that whether a prior art reference is material, i.e., whether there is a substantial likelihood that a reasonable examiner would have considered the reference important in deciding whether to allow the application to issue as a patent, is not controlled by whether that reference actually anticipates the claimed invention or would have rendered it obvious."); *Gardco Mfg., Inc. v. Herst Lighting Co.*, 820 F.2d 1209, 1213 (Fed. Cir. 1987) ("While Peerless argues that inequitable conduct should not be found absent unpatentability, that is not the standard this court has adopted....The simple fact is that a patent may be valid and yet unenforceable for...inequitable conduct."); *A.B. Dick Co. v. Burroughs Corp.*, 798 F.2d 1392, 1397 (Fed. Cir. 1986) ("[T]he test for materiality is *not* whether there is

anticipation or obviousness but, rather, what a 'reasonable examiner would consider important...in deciding whether to allow the application to issue as a patent.").

Finally, there is no merit to Purdue's argument that the controlled-release codeine formulation and U.S. Patent No. 4,834,984 ("the '984 patent) for controlled-release dihydrocodeine were cumulative or less pertinent than the art that was cited. (*Id.*) These formulations were not cumulative because they represented two additional controlled-release opioid compositions (beside hydromorphone) that exhibit 12-hour pain relief when the T_{max} is 2-4 hours. (Howard Decl., Ex. 17, DTX 2706; Ex. 13, DTX 2047, the '984 patent at col. 2. lns. 18-21.) A reference is cumulative only if it teaches no more than what a reasonable examiner would consider to be taught by the prior art already before the Patent Office. *Elk Corp. of Dallas v. GAF Building Materials Corp.*, 168 F.3d 28, 31 (Fed. Cir. 1999) (finding undisclosed prior art patents not cumulative where there were differences between the teachings of the disclosed prior art and the undisclosed prior art). But the controlled-release codeine and dihydrocodeine formulations teach *more* than the prior art of which the examiner was already aware. They teach that despite their structural differences—which Purdue argues makes "each opioid...different"—these formulations provide the same pain-relief profile with the same early T_{max} as their opioid siblings. In addition, this information is at odds with Purdue's express representation that a 4-8 hour T_{max} is typical. (Howard Decl., Ex. 27, PTX 7 at '331-7.) Thus, the information is not cumulative and Purdue had a duty to disclose it.

IV. Purdue's attorneys' failure to disclose the '598 patent in their applications for the '331 and '912 patents provides confirming evidence of an overall pattern of deceptive intent.

When, on November 21, 1991, attorney Steinberg filed the application for the '331 patent, he elected to disclose Purdue's '341 patent on controlled-release hydrocodone as pertinent prior art and then distinguished the inventors' controlled-release oxycodone from this

prior art. (Howard Decl., Ex. 24, DTX 2044, '331 patent, col. 1, lines 35-46) Steinberg had drafted and prosecuted not only the '341 patent on controlled-release hydromorphone, but also Purdue's '598 patent on controlled-release oxycodone. (Howard Decl., Ex. 2, *Endo* Tr. at 1608:4-20; Ex. 23, DTX 2048; Ex. 27, PTX 7 at '331-5 - '331-6.) It is difficult to see how Steinberg, consistent with his duty of candor and honesty, could decide that, in drafting a patent application for controlled-release oxycodone, it was appropriate to disclose the '341 patent on a *different* controlled-release opioid, while also deciding not to disclose the '598 patent on controlled-release oxycodone compositions.

The examiner independently found the '598 patent and, in an office action mailed on April 30, 1992, asserted the '598 patent as one of the prior-art patents that supported his rejection of the '331 claims as invalid for obviousness. (Howard Decl., Ex. 27, PTX 7 at '331-34 - '331-37.) Attorney Davidson undertook to prepare and file Purdue's response to this action in or around late October 1992. (*Id.* at '331-38 - '331-43.) At about the same time, Davidson was preparing the application for the '912 patent, which he filed (as a PCT application) on November 25, 1992. (Howard Decl., Ex. 39, PTX 4 at '912-100–'912-104.) Davidson clearly knew that the examiner in the '331 case considered the '598 patent to be a highly material prior-art reference. Yet in drafting the '912 application, Davidson described the '341 controlled-release hydromorphone patent but not the '598 oxycodone patent—just as was done in the '331 application—although Davidson did later file an information disclosure statement noting the '598 patent.

Purdue argues that the failure to disclose the '598 patent during its prosecution of the '331 patent cannot constitute inequitable conduct because of the examiner's independent discovery of this reference, citing this Court's decision in *Purdue Pharma L.P. v. Boehringer-*

Ingelheim GmbH, 98 F. Supp. 2d 362, 396 (S.D.N.Y. 2000), *aff'd*, 237 F.3d 1359 (2001). This proposition, however, is not necessarily valid. *See A.B. Dick Co.*, 798 F.2d at 1396-98 (finding inequitable conduct where applicants failed to disclose a reference of which they were aware notwithstanding that examiner discovered the reference on his own). The failure to cite the '598 patent in the '331 application was material, and is another manifestation of the deceptive intent with which the inventors and their attorneys approached and prosecuted the applications.

V. Purdue's failure to disclose contrary clinical data in its applications for the patents-in-suit constitutes further evidence of inequitable conduct.

Mallinckrodt established in its brief that Purdue withheld data from several clinical studies that showed results contrary to assertions that Purdue had made in its patents. (Mallinckrodt Br. at 31-32.) What Purdue doesn't say in connection with these studies is more revealing than what it does say. Purdue does not dispute that Kaiko, who reviewed these studies, knew of these conflicting results before the patents-in-suit issued. Nor does Purdue ever explain why a reasonable examiner would not have considered it important in deciding whether to allow the application. (*See* Purdue Br. at 35-39.)

Instead, Purdue is reduced to trying to downplay the importance of these studies. Its efforts in this regard fail. Each of the patents-in-suit states that "[i]t is yet another object of the present invention to provide a method for substantially reducing the time and resources need[ed] to titrate patients requiring pain relief on opioid analgesics." (*See* Howard Decl., Ex. 29, the '912 patent at col. 2, lns. 9-12; Ex. 30, the '295 patent at col. 2, lns. 9-12; Ex. 31, the '042 patent at col. 2, lns. 12-15; *see also* Howard Decl., Ex. 27, PTX 7 at '331-42.) Yet the only clinical data available—the LoRusso and Kalso and Reder studies—was actually contrary to Purdue's assertion. (Howard Reply Decl., Ex. 56 PTX 717 at P 187373, 187408 (LoRusso study, finding that OxyContin® is not easier to titrate that MS Contin®); Ex. 57, PTX 475 at P 275688 (Kalso

study, finding that the median number of days to achieve stable pain control was not significantly different with OxyContin® than with MS Contin®).) Purdue offers no reason for why a reasonable examiner would not consider this data important.

Furthermore, each of the patents in suit asserts that the invention reduces the dosage range by half. Again, the only clinical data available bearing on this assertion was from the LoRusso and Kalso studies, which showed that the dosage ranges for MS Contin® and OxyContin® were similar. (Howard Reply Decl., Ex. 56 PTX 717 at Table 5.1.1A, P 187442, P 187412; Ex. 57, PTX 475 at Table 5A, P 275725.) The results of these clinical studies—which Purdue relied on and submitted to FDA—contradicted Purdue's assertion that the dosage range for extended-release oxycodone was half that of other opioids. (*See* Howard Decl., Ex. 29, the '912 patent at col. 4, lns. 51-58; Ex. 30, the '295 patent at col. 4, lns. 51-58; Ex. 31, the '042 patent at col. 4, lns. 53-60 (each stating "other opioid analgesics require[ ] approximately twice the dosage range.") These test results were highly material precisely because they constituted information that was contrary to Purdue's arguments in favor of patentability of its controlled-release oxycodone claims, and a reasonable patent examiner would have found them important in considering whether to issue the patent. *See Cargill, Inc.v. Canbra Foods, Ltd.*, 476 F.3d 1359, 1366 (Fed. Cir. 2007) ("A reasonable examiner would certainly want to consider test data that is directly related to an important issue of patentability.")

Purdue's efforts to discredit this study data fails. It is irrelevant that this Court in *Endo* said—*with respect to infringement*—that "it is not clear what dosage range conclusions can be drawn from these studies." (Purdue Br. at 35-36.) The issue here is inequitable conduct, and Purdue withheld from the patent office the only comparative evidence that it had with respect to dosage ranges for controlled-release oxycodone and controlled-release morphine—evidence that

was inconsistent with its arguments for patentability. Yet Purdue submitted this same evidence to FDA to support its application for approval to sell its controlled-release oxycodone.

Purdue's next assertion—that non-disclosure was okay because "cancer patients who were already taking opioids to control their pain" are "unique"—is absurd. (Purdue Br. at 37.) A major indication for the use of controlled-release oxycodone is to alleviate pain in cancer patients. Indeed, one need look no further than to Kaiko's own published articles to know that cancer patients are perhaps the most commonly studied demographic for use of opioids in the treatment of chronic pain. (*See* Howard Reply Decl., Ex. 58 (Kaiko's article, titled "The United States Experience with Oral Controlled-Release Morphine: Review of Nine Dose Titration Studies…in Normal Subjects" reviewing the treatment of cancer-related pain who had been taking previous analgesics and citing at least 12 articles whose titles indicate a study of cancer patients taking opioid analgesics); *see also* Ex. 52, Ex. 59.) If, as Purdue claims, these studies were performed on an obscure demographic or not in accordance with the dosage range suggested by the patents, it makes little sense that Purdue would have submitted them to the FDA, let alone that FDA would have approved OxyContin® based on these studies. Purdue's submission of the clinical-study data to FDA at the same time as it withheld the data from the PTO is strong evidence of an intent to deceive.

Purdue's last argument states that because the LoRusso and Kalso studies never tested the "10-40 mg twice daily range discussed in the patents," the study results cannot be contrary to the patents. (Purdue Br. at 37.) To begin with, the premise of this argument is invalid: many patients in both studies did, in fact, take either 20 mg or 40 mg of Purdue's extended-release oxycodone twice daily—*exactly* as disclosed in the patent claims. (See Howard Reply Decl., Ex. 56, PTX 717 at Table 5.1.1A, P 187442, P 187387; Ex. 57, PTX 475 at Table 5A, P 275725,

P 275657.) The patent claims do not require administering the entire 10-40 mg range. Rather, the claims cover *any* dosage strength within that recited range, administered twice daily. (*See*, *e.g.*, Howard Decl., Ex. 31 the '042 patent at col. 20 lns. 18-21 ("A method for reduing the range in daily dosages required to control pain…comprising administering *an* oral dosage formulation…..") (emphasis added).)

Contrary to the statements in Purdue's brief, initial doses in the Kalso and LoRusso studies were not "dictated" by a protocol. Rather, they were *calculated* for each patient using opioid-equivalence ratios to estimate an effective dose of OxyContin®. (See Howard Reply Decl., Ex. 56, PTX 717 at P 187387-388; Ex. 57, PTX 475 at P 275658, P 275664-665.) The patient was then titrated to the appropriate dose to provide adequate pain relief without unacceptable side effects—consistent with good medical practice. (*Id.*) Purdue offers no evidence showing that just because the studies did not test every dosage within Purdue's prescribed four-fold range, information regarding titration of oxycodone and pain control cannot be discerned from these studies. These studies showed that there was no difference between OxyContin® and MS Contin®, yet Purdue withheld these studies from the PTO. (*See* Howard Reply Decl., Ex. 60, *Endo* Tr. at 420-21; Howard Decl., Ex. 35, DTX 4358 at P 572294).

Purdue's claim that these studies are representative of neither the invention in the patents nor a safe "real world" use of its drug product is balderdash. Purdue submitted these studies to FDA to show that this drug could be safely and effectively used "[i]n the real world." (Purdue Br. at 37.) Purdue's actions speak louder than its litigation-inspired words in this instance.

If there were even a close question as to whether Purdue should have disclosed this clinical data to the Patent Office—and there certainly was not—then Purdue was required to err on the side of disclosure so that the examiner could have independently decided whether the

studies were relevant to patentability. *See Labounty Mfg., Inc. v. United States Int'l Trade Comm'n*, 958 F.2d 1066, 1076 (Fed. Cir. 1992) (intent is not negated because "[the inventor] and his attorney could reasonably have decided these devices did not have to be disclosed. On the contrary, that makes it all the more necessary that the devices should have been disclosed to the examiner. Close cases should be resolved by disclosure, not unilaterally by the applicant.")

VI. It was deceptive for Purdue to present Kaiko as an independent expert.

When, on March 9, 1993, Kaiko filed his declaration in the '331 case, responding to the examiner's second rejection of the '331 claims as obvious in light of the '341 and '598 patents, the declaration did not disclose the association between Kaiko's employer, Purdue, and Euro-Celtique, the assignee of the '331 application. (Howard Decl., Ex. 27, PTX 7 at '331-51–'331-56.) The declaration did not disclose that Kaiko had collaborated with the inventors named in the '331 application in developing controlled-release oxycodone. (*Id.*) And the declaration did not disclose that Kaiko was a named inventor in the related '912 application that had been filed a few months earlier. (*Id.*) Instead, the declaration described Kaiko in language calculated to lead a reader to believe that Kaiko was an independent expert. (*Id.*)

Thus, the examiner was deprived of information concerning Kaiko's deep interest in, and involvement with, the invention of the '331 application. To the contrary, the declaration left the examiner with the impression that the declarant was an unbiased expert.

Purdue has previously argued that Kaiko and Purdue's attorneys had no duty to disclose Kaiko's interest because, although the examiner had requested a declaration, he had not asked that it come from an independent source. But the Federal Circuit in *Nilssen v. Osram Sylvania, Inc.*, No. 2006-1550, 2007 U.S. App. LEXIS 23733 (Fed. Cir. Oct. 10, 2007), put this argument to rest. In that case, the patent applicant filed affidavits of a third party without disclosing that

party's affiliation with him. *Id.* at *4. The Federal Circuit affirmed a judgment of inequitable conduct:

> We conclude that the district court did not abuse its discretion in holding that Nilssen engaged in inequitable conduct…by submitting affidavits by Fiene in support of patentability, including points of distinction over prior art patents, without informing the examiner of the affiant's relationship to Nilssen. Even though the examiner did not raise a question about any such relationship, it is material to the examiner's evaluation of the credibility and content of affidavits to know of any significant relationship between an affiant and an applicant, *see Ferring B.V. v. Barr Labs., Inc.*, 437 F.3d 1181, 1187-88 (Fed. Cir. 2006); failure to disclose that relationship violated Nilssen's duty of disclosure.

Id. at *11-*12.

Purdue does not contest the materiality of the failure by Kaiko and his attorneys to identify his interest and Purdue's relationship with Euro-Celtique. The level of materiality was demonstrably high because the examiner would not withdraw his obviousness rejection based on the argument of Purdue's attorney, but withdrew his prior-art-based rejection only after requesting and receiving Kaiko's declaration. (Howard Decl., Ex. 27, PTX 7 at '331-84.)

Purdue nevertheless tries to raise the shadow of an issue with respect to the intent prong of inequitable conduct, implying that Steinberg and Davidson lacked sufficient knowledge of the relationship between Purdue and Euro-Celtique to impose on them a duty to disclose that relationship in Kaiko's declaration.

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Purdue also argues that, in any event, "[t]he PTO was made aware of the relationships between Dr. Kaiko and the '331 inventors and between Dr. Kaiko and Euroceltique." (Purdue Br. at 13, 32.) To support this argument, Purdue relies on the fact that the November 25, 1992 application that matured into the '912 patent was filed as a PCT international application, which triggered a requirement that the US PTO prepare an international search report on the prior art. (*Id.* at 13.) Purdue points out that the PCT application states that it is related to the application for the '331 patent, names *Euro-Celtique* as the assignee, and identifies Kaiko, along with the named inventors of the '331 patent, as the inventors of the PCT application. (*Id.* at 34-35.) Purdue also notes that the international search report identifies the examiner in the '331 prosecution, Spears, as the "authorized officer" for the search report. (*Id.*) Therefore, Purdue asserts, the examiner knew what he needed to know about Kaiko's interest and potential bias. (*Id.*)

Purdue's explanation does not withstand scrutiny. The international search report bears the *printed* name, James M. Spears, but it is signed by a different employee of the Patent Office, one Briggs. (Inz Decl., Ex. 6 at P 206099.) There is no assurance that Spears, not Briggs, actually conducted the prior-art search.

Moreover, even assuming Spears did the work, which would include a review of the specification in order to determine the nature and scope of the subject matter that needed to be searched, there is no reason to believe that he also combed other parts of the PCT application for

additional information on the identity of the inventors, the assignee, etc., that were irrelevant to his immediate purpose. And it taxes credibility past the breaking point to assume that examiner Spears would immediately remember these irrelevant details from a search report that issued in January 1993 when he received Kaiko's declaration in the '331 case four months later.

Finally, in a last effort to salvage its case, Purdue argues that the relationship between the inventor Oshlack and Kaiko regarding controlled-release oxycodone was revealed in Kaiko's curriculum vitae, which was attached to his declaration. (Purdue Br. at 34.) The CV contains a single-spaced list of 77 peer-reviewed articles and another single-spaced list of 115 published abstracts. (Howard Decl., Ex. 27, PTX 7 at 331-64–'331-77.) Purdue points out that eight of these publications identify Oshlack as a co-author, but fails to note that none of the eight publications relates to controlled-release oxycodone. (*Id.*) Purdue also fails to note that nearly every one of 180 other publications identifies numerous other persons as co-authors, with the same individuals often being identified in several publications. (*Id.*)

Purdue's unstated premise is that examiners must treat an applicant's submissions to the Patent Office like a detective story, combing each document for disconnected clues. The duty of candor and full disclosure destroys this premise. A patent examination is not an exercise in detection, as cases condemning the burying of relevant prior art references in long lists of other, irrelevant references establish. *See, e.g.*, *Molins PLC v. Textron, Inc.*, 48 F.3d 1172, 1183-84 (Fed. Cir. 1995) ("burying a particularly material reference in a prior art statement containing a multiplicity of other references can be probative of bad faith. *Cf.* MPEP § 2004, Item 13 (4th ed., rev. 5, Jan. 1981) ('Don't submit long lists of prior art if it can be avoided. Eliminate clearly irrelevant and marginally pertinent cumulative prior art. If a long list is submitted, highlight those references which may be of most significance.')").

VII. The pattern of multiple acts of deceptive misconduct in the Patent Office compels a judgment of unenforceability.

The final step that the Court must take in its analysis of the inequitable-conduct issue is to weigh the evidence on the materiality of the patentee's misrepresentations and/or omissions and the evidence of the patentee's intent to determine whether, as a matter of equity, a judgment of unenforceability is justified. *Cargill, Inc.*, 476 F.3d at 1364. In addressing this step in the inequitable-conduct analysis, Purdue focuses on the failure by the inventors and their counsel to tell the Patent Office that there was no empirical proof of the four-fold range. (Purdue Br. at 39-40.) Thus, Purdue again implies that this case involves solely the *Endo* remand.

This is *not* the *Endo* remand. Mallinckrodt has presented a disturbing pattern of highly material acts of deception in the Patent Office that, in combination, strongly establish an intent to deceive. Similar patterns of misconduct have frequently been found to evidence wrongful intent and to justify a judgment of unenforceability. *See, e.g., Paragon Podiatry Lab.*, 984 F.2d at 1193 ("The prosecution of the patent application in this case, viewed in its entirety, demonstrates an overriding pattern of misconduct sufficient to support the district court's finding of culpable intent."); *Ferring B.V. v. Barr Labs, Inc.*, 437 F.3d 1181, 1194 (Fed. Cir. 2006) (affirming the district court's equitable judgment of unenforceability based upon "multiple omissions over a long period of time—a fact that heightened the seriousness of the conduct."); *Golden Valley Microwave Foods*, 837 F. Supp. 1444, 1471 (N.D. Ind. 1992) ("The facts include too many instances of the withholding of material information for any conclusion to be reached other than that the withholding and mischaracterizations were done with the intent to mislead the Patent Office.")

It is evident that, from the outset, the inventors and their counsel set out to mislead the Patent Office by asserting that they had empirical data to demonstrate both the eight-fold dosage

range required to control pain in 90% of patients with prior-art opioids and the superior four-fold dosage range of controlled-release oxycodone.

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Moreover, Purdue does not try to justify the further, illicit use that its attorney Davidson made of the non-existent surveys during prosecution of the '331 application and the '912 application. In the '331 case, Davidson distinguished the product of the '341 controlled-release hydromorphone patent by stating, as a matter of established fact, that "controlled release hydromorphone" requires "the approximately eight-fold range" and that "[o]ne skilled in the art would certainly not arrive at th[e] surprising result [concerning oxycodone's dosage range] without the benefit of hindsight." (Howard Decl., Ex. 27, PTX 7 at '331-43) Davidson made essentially the same representation again in the '912 case. (Howard Decl., Ex. 39, PTX 4 at '912-124–'912-126.) While Purdue asserts that these representations played no causal role in the allowance of the patents, the examiner's statement of reasons for allowance of the '042 establishes that they did. (Howard Decl., Ex. 40, PTX 6 at '042-64.) Moreover, Purdue persists in making this factually insupportable argument to this Court in the face the Federal Circuit rejection of the argument, as a matter of law, in the *Endo* case. *Endo*, 438 F.3d at 1131-33.

The obvious decision by the inventors and their attorneys to misrepresent to the Patent Office that surveys of other opioid analgesics had been performed that documented the eight-fold dosage range also sheds damning light on their accompanying characterization of the four-fold

dosage range of the invention in words that implied the existence of clinical proof. These acts were not done separately. They were part of a piece.

The other acts of misconduct, the presentation of Kaiko as an independent, presumably disinterested expert in his declaration, the withholding of the only relevant clinical studies, the failure to inform the Patent Office that controlled release oxycodone was the *fifth* controlled release opioid to share the characteristics of an early T_{max} and 12 hours of therapeutic activity, and the failure to disclose the '598 patent in the applications for the patents in suit, are all part of the same piece.

A judgment of unenforceability is fully justified.

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